Attorney Docket No.: 3800024.00560 / 4207

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | | |
|---|---|---|---|
| Applicant | : Lawrence G. Hamann *et al.* | Art Unit | : 1624 |
| Patent No. | : 7,632,858 | Examiner | : Balasubramanian, Venkataraman |
| Issue Date | : December 15, 2009 | Conf. No. | : 9300 |
| Serial No. | : 10/712,456 | Cust. No. | : 77202 |
| Filed | : November 13, 2003 | | |
| Title | : OPEN CHAIN PROLYL UREA-RELATED MODULATORS OF ANDROGEN RECEPTOR FUNCTION | | |

**Attn: Certificate of Correction Branch**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**REQUEST FOR CERTIFICATE OF CORRECTION**

Dear Sir:

Pursuant to 37 C.F.R. 1.322 and 1.323, the patentee respectfully requests that a Certificate of Correction be issued for the above referenced patent to correct the following errors:

**IN THE TITLE PAGES:**

In Item (56) References Cited, please remove from the list of OTHER PUBLICATIONS the following duplicate references beginning on page 3, first column, line 35, through page 3, second column, line 11:

— Beyler et al., J. Am. Med. W. Assoc., 23(8):708-721 1968.—;

— Boeijen et al., Bioorg. Med. Chem. Lett. 8:2375-2380 1998.—;

— Boris et al., Steroids, 15:61-71 1970.—;

— Bundgaard, "Design of Prodrugs", Elsevier Science Publishers 1985, tabe of contents.—;

— Bundgaard, "Design and Application of Prodrugs", Harwood Academic Publishers 1991, pp. 113-191.—;

— Chalepakis et al., Cell, 53:371-382 1988.—;

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label Number: **EM 315450707US**
Date of Deposit: **January 28, 2010**
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Attn: Certificate of Correction Branch, Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Stefanie Dost

Stefanie Dost

— Delaisi et al., J. Steroid Biochem. Molec. Biol. 41(3-8)773-7 1992.—;

— Dyatkin Tet Lett 38(12):2065-6 1997.—;

— Edwards et al., Bioorg. Med. Chem. Lett 9: 1003-8 1999.—;

— Gori et al., Boll.-Soc. Ital. Boil. Sper. 42:1596-1599 1996.—;

— Gori et al., Boll.-Soc. Ital. Boil. Sper. 42:1600-1601 1996.—;

— Hamann et al., J. Med. Chem. 42(2):210-212 1998.—;

— Heiser, in Methods in Mol. Biol. 130:117-134 2000.—;

— Hempstock et al., J. Med. Food 2(3-4):243-246 1999.—;

— Hershberger et al., P.S.E.B.M. 83:175-180 1953.—;

— Hiroaka et al., Cancer Res., 47:6560-6564 1987.—;

— Imakura et al., Chem. Pharm. Bull. 40(7): 1691-1696 1992.—;

— Iseki, K. et al., Tet. 53(10) 3513-26 1997.—;

— Issartel et al., 1996, CAS 125:316198.—;

— Johannsson et al., J. Clin. Endocr. Met. 82(3):727-734 1997.—;

— Kakigami et al., Chem. Pharm. Bull. 46(1):42-52 1998.—;

— Lalezari et al., J Het Chem 20(2) 483-485 (1983).—;

— Matsuki et al., Chem. Pharm. Bull. 42(1):9-18 1994.—;

— Milata et al., Org. Prep. Proc. Int'l, 25(6):703-704 1993.—;

— Minesita et al., Cancer Research 25:1168-1175 1965.—;

— Navone et al., Clin. Canc. Res. 3:2493-2500 1997.—;

— Okuda et al., J. Urology 145:188-191 1991.—;

— Palovich et al., 2000, CAS 134:25357.—;

— Panouse et al., Ann. Pharm. Franc., 2000:291-302.—;

— Rodbard in Ligand Assay, Masson Publishing USA Inc., 1981, pp. 45-101.—;

— Schuur et al., J. Biol. Chem. 271(12):7043-7051 1996.—;

— Suzuki et al., J. Steroid Chem. Mol. Biol. 37(4):559-567 1990.—;

— Talon et al., Br. J. Pharmacol., 134(7): 1523-31 2001.—;

— Montes de Oca et al., Arkivoc, 390-403 (2003).—;

— Uozumi, Tet Lett 42:407-410 2001.—;

— Uozumi et al., Tet Lett 42:411-414 2001.—;

— Venable, Am. J. Anat. 119:263-270 1966.—; and

— Wermuth et al. In the Practice of Medicinal Chemistry, Academic Press, 1996, pp. 671-696.—.

In Item (56) References Cited, please remove from the list of OTHER PUBLICATIONS the following duplicate references beginning on page 3, second column, line 53, through page 3, second column, line 62:

— U.S. Appl. No. 11/048,439, Filed Feb. 1, 2005, Publ. No. 2005-0187267.—;

— U.S. Appl. No. 11/070,808, Filed Mar. 2, 2005, Publ. No. 2005-0197359.—;

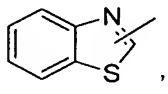
— U.S. Appl. No. 11/931,282, Filed Oct. 31, 2007, Publ. No. 2008-0108649.—;

— U.S. Appl. No. 11/931,395, Filed Oct. 31, 2007, Publ. No. 2008-0103188.—; and

— U.S. Appl. No. 11/931,498, Filed Oct. 31, 2007, Publ. No. 2008-0108691.—;

**IN THE SPECIFICATION:**

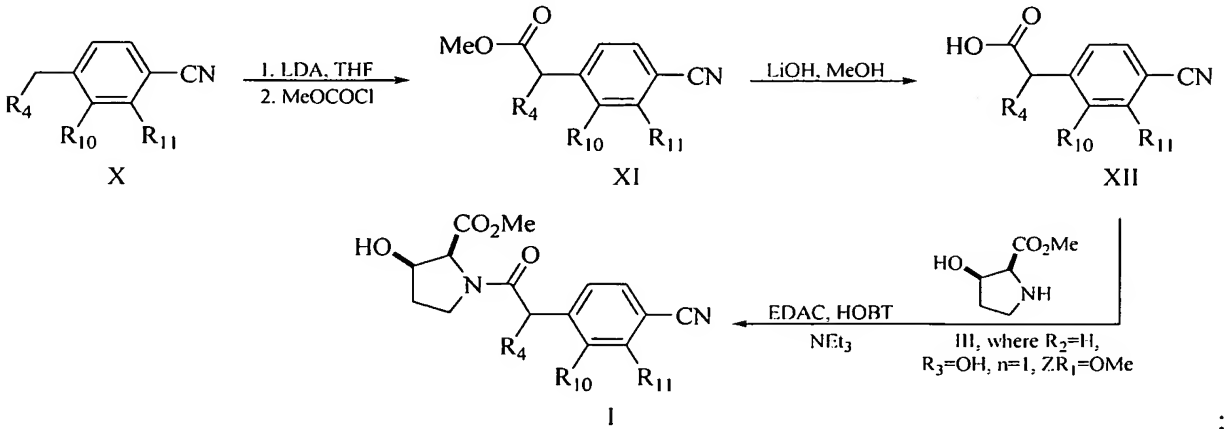
In column 8, beginning at line 25, please replace the structure of the eighth heteroaryl group listed with:



;

in column 13, line 10, please replace "V" with –VI–;

in columns 13-14, beginning at line 41, please replace the designator "XI" with –XII– for the third chemical structure in Scheme V as shown below:




X XI XII I

;

in column 20, lines 29-30, please replace "Tibo lone, pro stanoids" with –Tibolone, prostanoids–;

in column 20, line 44, please replace "famesyl" with –farnesyl–;

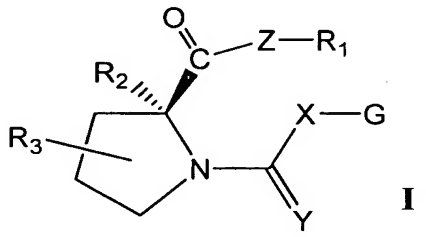
in column 32, line 2, please replace "(85%),. column" with –(85%), column–;

in column 36, line 14, please replace "mmol):,in" with –mmol) in–;

**IN THE CLAIMS:**

Please replace Claims 1 and 12 with the following Claims:

1. A compound of formula I




I

or a pharmaceutically acceptable salt thereof,

wherein:

$R_1$ is selected from the group consisting of alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

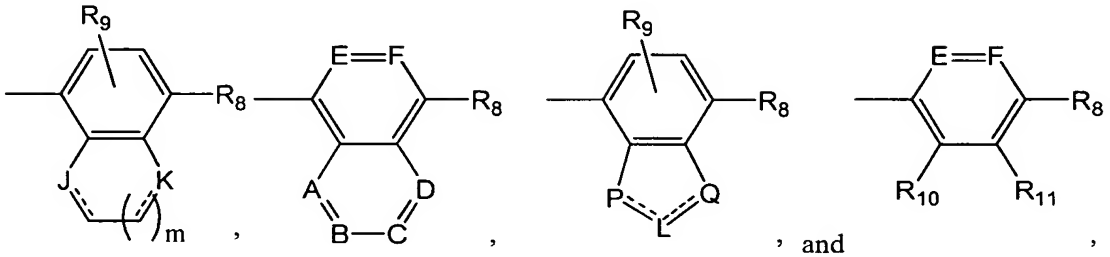
$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocycle or substituted heterocycle, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CH_2OR_4$, $OR_2$, $SR_2$, halo, $NHR_2$, $NHCOR_4$, and $NHCONR_4R_4'$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and

heteroaryl or substituted heteroaryl;

G is selected from among:



, and ,

wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and $CR_l$;

J, K, L, P, and Q each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_l$;

m is an integer of 0 or 1 ;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and

Z is –O–[[,]] or $NR_4$;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_l$ is methyl,

X is NH, and

Y is O or S, then

Z is not O;

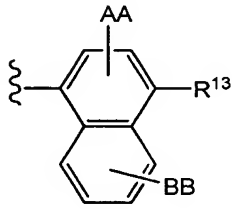
(c) when (i) $R_l$ is methyl,

(ii) X is NH,

(iii) Y is $NR_4$,

(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro ($-NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, [[~~$SO_2NR_{15}NR_{15}$'~~]] $SO_2NR_{15}R_{15}$', $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group is independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

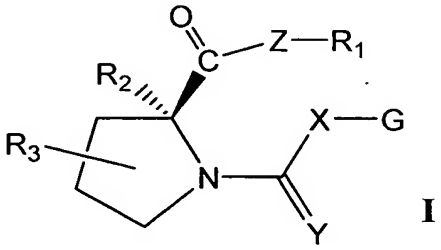
$R_{15}$ and $R_{15}$' in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and -CN;

AA and BB each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro ($-NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

12. A compound of formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

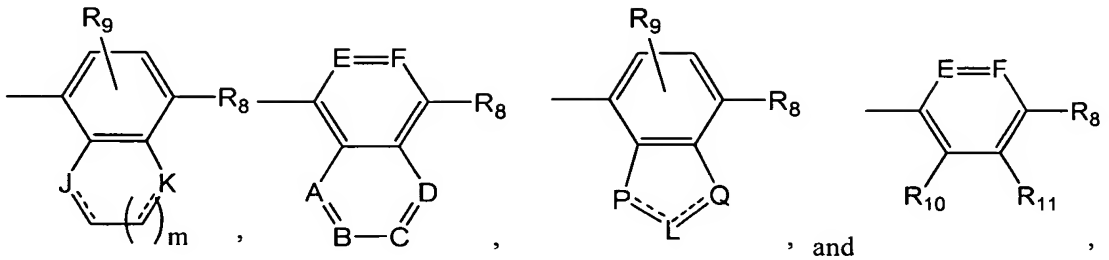
$R_1$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of alkyl or substituted alkyl, and [[~~$CH_2R_4$~~]] $\underline{CH_2OR_4}$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from the group consisting of:




wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and $CR_1$;

J, K, L, P, and Q each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$;

m is an integer of 0 or 1 ;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and

Z is –O-[[,]] or $NR_4$;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_1$ is methyl, X is NH, and Y is O or S, then Z is not O;

(c) when

(i) $R_1$ is methyl,

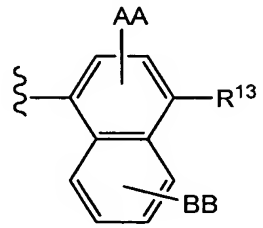
(ii) X is NH,

(iii) Y is $NR_4$,

(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl,

arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro ($-NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, [[~~$SO_2NR_{15}NR_{15}$'~~]] $SO_2NR_{15}R_{15}$', $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group independently is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

$R_{15}$ and $R_{15}$' in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and CN;

AA and BB each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro ($-NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

## REMARKS

A Certificate of Correction incorporating the above changes is included with this Request. Since the errors are those of the Patent Office, no fee should be due. If it is determined that a fee is due, the Office is hereby authorized to charge the fee to Deposit Account No. 02-1818.

This Certificate of Correction seeks to remove duplicate publications listed in the "OTHER PUBLICATIONS" section of References Cited, Item (56). Publications "Beyler et al." through "Wermuth et al." (page 3, column 1, line 35, through page 3, column 2, line 11) are previously listed (page 2, column 2, line 66, through page 3, column 1, line 34). The U.S. Publication Nos. are previously listed in the "U.S. PATENT DOCUMENTS" section beginning on page 2, column 1, line 8.

This Certificate of Correction seeks to correct numerical, formatting, spelling and chemical structure errors in the Specification introduced by the PTO. The error in the heteroaryl group structure in column 8, beginning at line 25, is corrected by replacing an "N" with an "S" in the structure of the eighth heteroaryl group listed. The error in column 13, line 10, is corrected by replacing "V" with "VI." The error in Scheme 5 at columns 13 and 14, beginning at line 41, is corrected by replacing "XI" with "XII" for the third chemical structure in the scheme. The errors in column 20, lines 29-30 are corrected by deleting the extra spaces in the words "Tibo lone, pro stanoids" so that it now reads "Tibolone, prostanoids." The spelling error in column 20, line 44, is corrected by replacing "famesyl" with "farnesyl." The punctuation error in column 32, line 2, is corrected by deleting the period "." in "(85%),. column" so that it now reads "(85%), column." The punctuation error in column 36, line 14, is corrected by deleting the colon and comma ":," in "mmol):,in" so that it now reads "mmol) in."

This Certificate of Correction seeks to correct omissions, punctuation and spelling errors in the Claims. The error in Claim 1 at column 37, line 21 (which was previously amended in the Amendment mailed on April 9, 2009, a copy of which is attached herewith as evidence), is corrected by adding a colon ":" after "wherein."

The punctuation error introduced by the PTO in Claim 1 at column 37, line 41, is corrected by deleting the comma "," after "–O– ."

The error in Claim 1 at column 38, line 5 (which was previously amended in the Amendment mailed on October 7, 2009, a copy of which is attached herewith as evidence), is corrected by replacing "$SO_2NR_{15}NR_{15}$'" with "$SO_2NR_{15}R_{15}$'."

The error in Claim 12 at column 39, line 48, is corrected by replacing "$CH_2R_4$" with "$CH_2OR_4$." Issued Claim 12 is original Claim 15, added in the Amendment submitted on April 18, 2008, a copy of which is attached herewith as evidence.

The punctuation error introduced by the PTO in Claim 12 at column 40, line 33, is corrected by deleting the comma "," after "–O– ."

The error in Claim 12 at column 40, line 64 (which was previously amended in the Amendment mailed on October 7, 2009, a copy of which is attached herewith as evidence), is corrected by replacing "$SO_2NR_{15}NR_{15}$'" with "$SO_2NR_{15}R_{15}$'."

This Certificate of Correction seeks to amend these errors in the Title Pages, Specification and Claims introduced by the Patent and Trademark Office. These changes do not constitute new matter. Patentee respectfully requests correction of these errors by issuance of a Certificate of Correction.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 3800024.00560 / 4207
**Address all correspondence to:** 77202
Stephanie Seidman
K&L Gates LLP
3580 Carmel Mountain Road, Suite 200
San Diego, California 92130
Telephone: (858) 509-7410
Facsimile: (858) 509-7460
email: stephanie.seidman@klgates.com

NEW CERTIFICATE OF CORRECTION

Staple Here Only

# UNITED STATES PATENT AND TRADEMARK OFFICE
# CERTIFICATE OF CORRECTION



PATENT NO. .: 7,632,858 B2

APPLICATION NO .: 10/712,456

DATED .: DECEMBER 15, 2009

INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

**IN THE TITLE PAGES:**

In Item (56) References Cited, please remove from the list of OTHER PUBLICATIONS the following duplicate references beginning on page 3, first column, line 35, through page 3, second column, line 11:

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— Hamann et al., J. Med. Chem. 42(2):210-212 1998.—;
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— Hershberger et al., P.S.E.B.M. 83:175-180 1953.—;
— Hiroaka et al., Cancer Res., 47:6560-6564 1987.—;

MAILING ADDRESS OF SENDER:

Stephanie Seidman
K&L Gates LLP
3580 Carmel Mountain Road, Suite 200
San Diego, CA, 92130

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# UNITED STATES PATENT AND TRADEMARK OFFICE
## CERTIFICATE OF CORRECTION



PATENT NO. .: 7,632,858 B2

APPLICATION NO .: 10/712,456

DATED .: DECEMBER 15, 2009

INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

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MAILING ADDRESS OF SENDER:

Stephanie Seidman
K&L Gates LLP
3580 Carmel Mountain Road, Suite 200
San Diego, CA, 92130

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# UNITED STATES PATENT AND TRADEMARK OFFICE
## CERTIFICATE OF CORRECTION



PATENT NO. .: 7,632,858 B2

APPLICATION NO .: 10/712,456

DATED .: DECEMBER 15, 2009

INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

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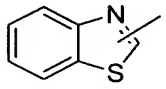
— U.S. Appl. No. 11/931,282, Filed Oct. 31, 2007, Publ. No. 2008-0108649.—;
— U.S. Appl. No. 11/931,395, Filed Oct. 31, 2007, Publ. No. 2008-0103188.—; and
— U.S. Appl. No. 11/931,498, Filed Oct. 31, 2007, Publ. No. 2008-0108691.—;

**IN THE SPECIFICATION:**

In column 8, beginning at line 25, please replace the structure of the eighth heteroaryl group listed with:



';

in column 13, line 10, please replace "V" with –VI–;

MAILING ADDRESS OF SENDER:

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K&L Gates LLP
3580 Carmel Mountain Road, Suite 200
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# UNITED STATES PATENT AND TRADEMARK OFFICE
## CERTIFICATE OF CORRECTION



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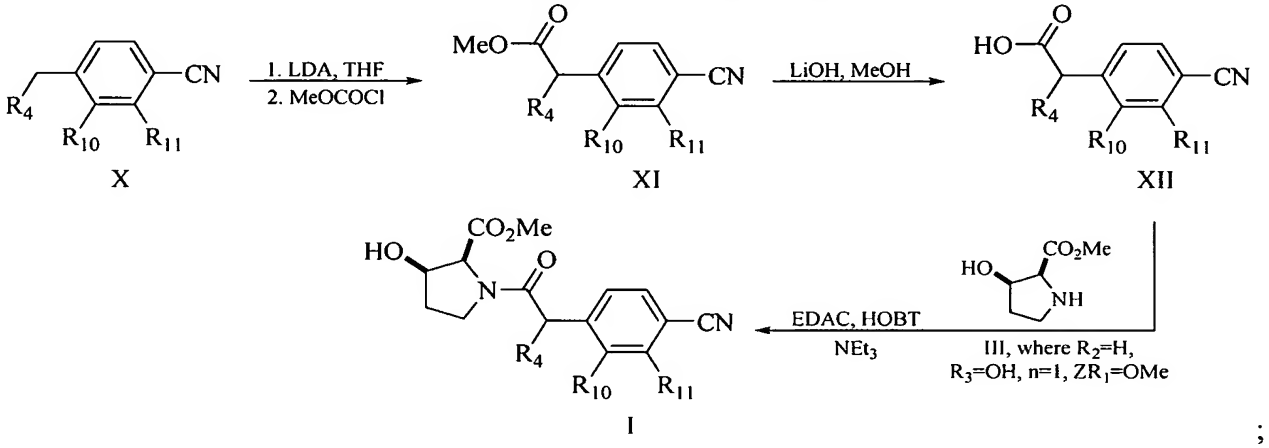
APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

in columns 13-14, beginning at line 41, please replace the designator "XI" with –XII– for the third chemical structure in Scheme V as shown below:




;

in column 20, lines 29-30, please replace "Tibo lone, pro stanoids" with –Tibolone, prostanoids–;
in column 20, line 44, please replace "famesyl" with –farnesyl–;
in column 32, line 2, please replace "(85%),. column" with –(85%), column–;
in column 36, line 14, please replace "mmol):,in" with –mmol) in–;

MAILING ADDRESS OF SENDER:

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# UNITED STATES PATENT AND TRADEMARK OFFICE
# CERTIFICATE OF CORRECTION

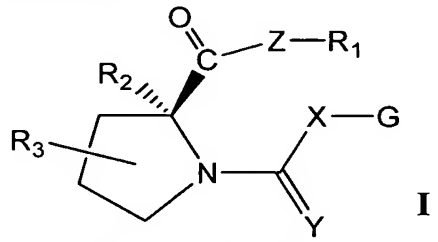


PATENT NO. .: 7,632,858 B2
APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

**IN THE CLAIMS:**
Please replace Claims 1 and 12 with the following Claims:

1. A compound of formula I




I

or a pharmaceutically acceptable salt thereof,
wherein:

$R_1$ is selected from the group consisting of alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocycle or substituted heterocycle, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CH_2OR_4$, $OR_2$, $SR_2$, halo, $NHR_2$, $NHCOR_4$, and $NHCONR_4R_4'$;

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## CERTIFICATE OF CORRECTION

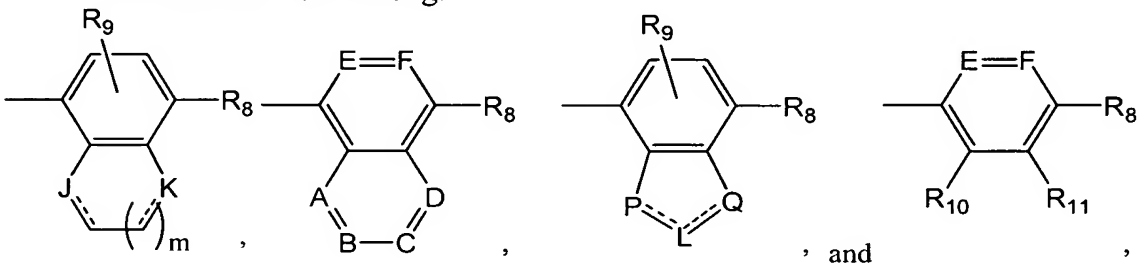


PATENT NO. .: 7,632,858 B2
APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from among:




, , , and ,

wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and $CR_1$;

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## CERTIFICATE OF CORRECTION



PATENT NO. .: 7,632,858 B2
APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

J, K, L, P, and Q each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$;

m is an integer of 0 or 1 ;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and

Z is –O– or $NR_4$;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_1$ is methyl,
X is NH, and
Y is O or S, then
Z is not O;

(c) when (i) $R_1$ is methyl,
(ii) X is NH,
(iii) Y is $NR_4$,
(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or

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# UNITED STATES PATENT AND TRADEMARK OFFICE
# CERTIFICATE OF CORRECTION

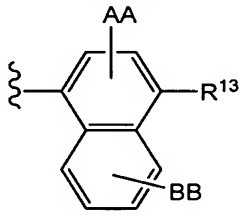


PATENT NO. .: 7,632,858 B2
APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-$NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, $SO_2NR_{15}R_{15}'$, $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group is independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

$R_{15}$ and $R_{15}'$ in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and -CN;

AA and BB each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro (-$NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

P is an integer from 0 to 2,

then Z is not O.

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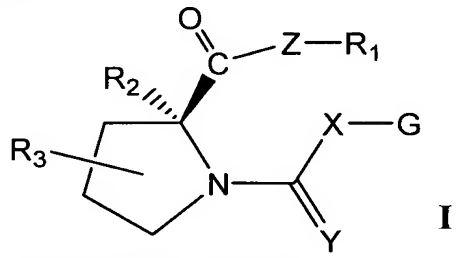
# UNITED STATES PATENT AND TRADEMARK OFFICE
## CERTIFICATE OF CORRECTION



PATENT NO. .: 7,632,858 B2
APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

12. A compound of formula I




I

or a pharmaceutically acceptable salt thereof,

wherein:

$R_1$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of alkyl or substituted alkyl, and $CH_2OR_4$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or

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PATENT NO. .: 7,632,858 B2
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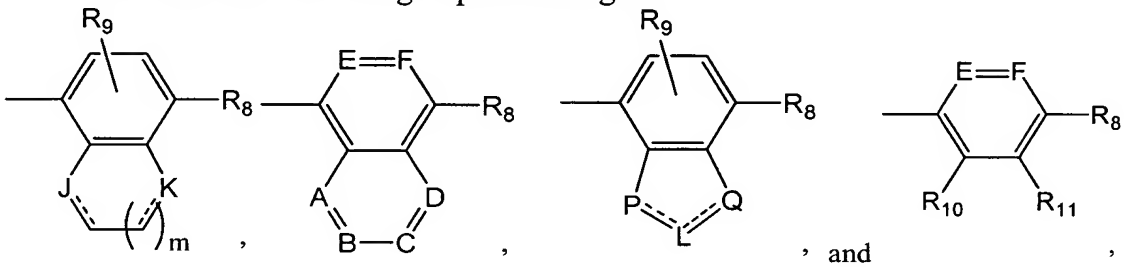
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from the group consisting of:




, , , and ,

wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and $CR_1$;

J, K, L, P, and Q each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$;

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APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

m is an integer of 0 or 1 ;
X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;
Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and
Z is –O– or $NR_4$;
with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;
(b) when $R_1$ is methyl, X is NH, and Y is O or S, then Z is not O;
(c) when
  (i) $R_1$ is methyl,
  (ii) X is NH,
  (iii) Y is $NR_4$,
  (iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and
  (v) G has the following structure:

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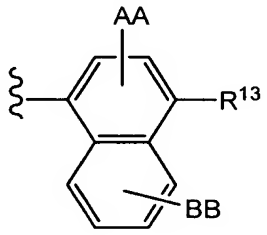
# UNITED STATES PATENT AND TRADEMARK OFFICE
## CERTIFICATE OF CORRECTION



PATENT NO. .: 7,632,858 B2
APPLICATION NO .: 10/712,456
DATED .: DECEMBER 15, 2009
INVENTOR(S) .: LAWRENCE G. HAMANN *ET AL.*

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-$NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, $SO_2NR_{15}R_{15}'$, $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group independently is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

$R_{15}$ and $R_{15}'$ in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and CN;

AA and BB each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro (-$NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

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PRELIMINARY AMENDMENT AND REQUEST FOR CONTINUED EXAMINATION
DATED 09 APRIL 2009

Attorney's Docket No.: 0119378-00560 / 4207

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | | |
|---|---|---|---|
| Applicant | : Hamann *et al.* | Art Unit | : 1624 |
| Serial No. | : 10/712,456 | Examiner | : V. Balasubramanian |
| Filed | : November 13, 2003 | Confirm. No.: | 9300 |

Title : **OPEN-CHAIN PROLYL UREA-RELATED MODULATORS OF ANDROGEN RECEPTOR FUNCTION**

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**PRELIMINARY AMENDMENT AND REQUEST FOR CONTINUED EXAMINATION (RCE)**

Dear Sir:

This preliminary amendment is filed with a Request for Continued Examination (RCE) of the above-captioned application. Entry of the following amendments and consideration of the following remarks are respectfully requested.

**Amendments to the claims** are reflected in the listing of the claims, which begin on page 2 of this paper.

**Remarks/Arguments** begin on page 10 of this paper.

A **Supplemental Information Disclosure Statement** accompanies this response.

**CERTIFICATE OF MAILING BY "EXPRESS MAIL"**
"Express Mail" Mailing Label Number EM 315453884 US
Date of Deposit: April 9, 2009
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Mail Stop RCE, Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

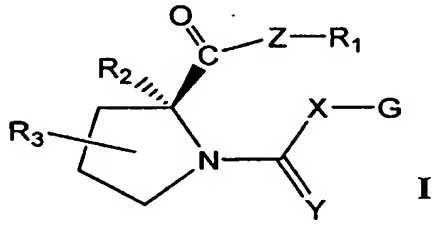
Christopher Ochs

**AMENDMENTS TO THE CLAIMS:**

Claims 1, 4-8 and 10-19 are pending. Please amend claim 1, 4-8 and 11-19 as indicated below. This listing of claims replaces all prior versions and listings of claims in the application.

**LISTING OF CLAIMS:**

1. (Currently amended) A compound of the formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

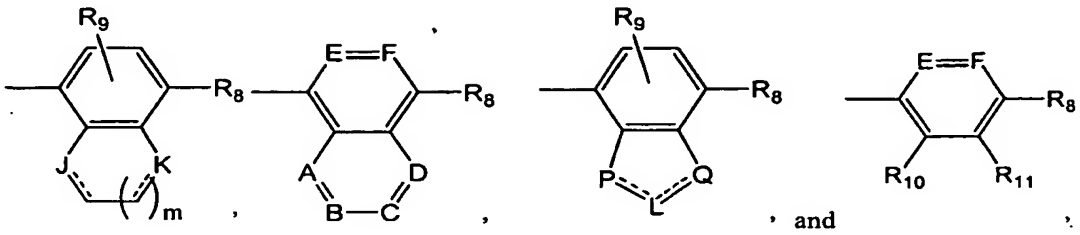
$R_1$ is selected from the group consisting of alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocycle or substituted heterocycle, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CH_2OR_4$, $OR_2$, $SR_2$, halo, $NHR_2$, $NHCOR_4$, and $NHCONR_4R_4'$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from the group of:




wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F ~~are~~ each independently is selected from among N and $CR_1$;

J, K, L, P, and Q ~~are~~ each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$;

m is an integer of 0 or 1 ;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and

Z is –O- or $NR_4$;

with the following provisos:

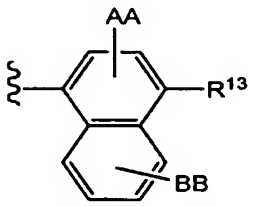
(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_1$ is methyl,
X is $NH_2$ [[;]] and
Y is O or S, then
Z is not O;

(c) when (i) $R_1$ is methyl,
(ii) X is NH,
(iii) Y is $NR_4$,

(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro ($-NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, $SO_2NR_{15}NR_{15}'$, $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group is independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

$R_{15}$ and $R_{15}'$ in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and -CN;

AA and BB ~~are~~ each independently <u>is</u> selected from the group consisting of hydrogen, halo, cyano (-CN), nitro ($-NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

2. (Cancelled).

3. (Cancelled).

4. (Currently amended) The compound ~~as defined in~~ of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

$R_1$ is alkyl;

$R_2$ is hydrogen or alkyl;

$R_3$ is hydroxyl;

Y is O; and

Z is O.

5. (Currently amended) A pharmaceutical composition, comprising:

a compound or salt ~~as defined in~~ of claim 1; and

a pharmaceutically acceptable carrier therefor.

6. (Currently amended) The pharmaceutical composition ~~as defined in~~ of claim 5, further comprising a growth promoting agent.

7. (Currently amended) A pharmaceutical composition, comprising:

a compound ~~as defined in~~ of claim 1, or a pharmaceutically acceptable salt thereof, and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

8. (Currently amended) A method for treating prostate cancer, comprising: ~~which comprises~~ administering to a mammalian species in need of treatment an effective amount of a compound ~~as defined in~~ of claim 1 or a pharmaceutically acceptable salt thereof.

9 (Cancelled).

10. (Previously presented) A compound selected from the group consisting of

1-(4-Cyano-2-ethyl-3-(trifluoromethyl)phenyl-1-carbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid or a pharmaceutically acceptable salt thereof;

1-(4-Cyanonaphthalen-1-ylcarbamoyl-3-hydroxy-pyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof;

1-(5-Chloro-6-cyano-pyridin-3-ylcarbamoyl)-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof; and

1-[2-(4-Cyanonaphthalen-1-yl)acetyl]-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof.

11. (Currently amended) A pharmaceutical composition, comprising:

a compound ~~as defined in~~ of claim 10, or a pharmaceutically acceptable salt thereof; [[,]] and a pharmaceutically acceptable carrier therefor.

12. (Currently amended) The pharmaceutical composition ~~as defined in~~ of claim 11, further comprising a growth promoting agent.

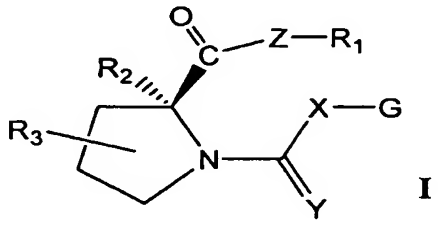
13. (Currently amended) A pharmaceutical composition, comprising:

a compound ~~as defined in~~ of claim 10, or a pharmaceutically acceptable salt thereof; [[,]] and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

14. (Currently amended) A method for treating prostate cancer, comprising: ~~which comprises~~ administering to a mammalian species in need of treatment an effective amount of a compound ~~as defined in~~ of claim 10 or a pharmaceutically acceptable salt thereof.

15. (Currently amended) A compound of formula I




I

or a pharmaceutically acceptable salt thereof,

wherein:

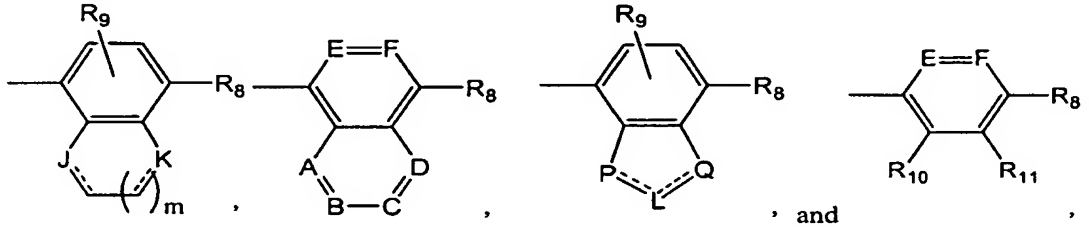
$R_1$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of alkyl or substituted alkyl, and $CH_2OR_4$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from the group consisting of:




, , , and ,

wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F ~~are~~ each independently is selected from among N and $CR_1$;

J, K, L, P, and Q ~~are~~ each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$;

m is an integer of 0 or 1 ;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and

Z is –O- or $NR_4$;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_1$ is methyl, X is NH, and Y is O or S, then Z is not O;

(c) when

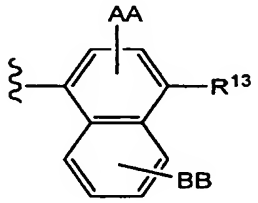
(i) $R_1$ is methyl,

(ii) X is NH,

(iii) Y is $NR_4$,

(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro ($-NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, $SO_2NR_{15}NR_{15}'$, $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group ~~is~~ independently is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

$R_{15}$ and $R_{15}'$ in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or

substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and CN;

AA and BB ~~are~~ each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro ($-NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

16. (Currently amended) A pharmaceutical composition, comprising:

a compound ~~as defined in~~ of claim 15, or a pharmaceutically acceptable salt thereof; [[,]] and

a pharmaceutically acceptable carrier therefor.

17. (Currently amended) The pharmaceutical composition ~~as defined in~~ of claim 16, further comprising a growth promoting agent.

18. (Currently amended) A pharmaceutical composition, comprising:

a compound ~~as defined in~~ of claim 15, or a pharmaceutically acceptable salt thereof; [[,]] and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

19. (Currently amended) A method for treating prostate cancer, comprising:

~~which comprises~~ administering to a mammalian species in need of treatment an effective amount of a compound ~~as defined in~~ of claim 15 or a pharmaceutically acceptable salt thereof.

## REMARKS

The requisite fee for filing a Request for Continued Examination and any other fees that may be due in connection with the filing of this paper or with this application should be charged to Deposit Account No. 02-1818. If a Petition for Extension of Time is needed, this paper is to be considered such Petition. A supplemental Information Disclosure Statement is filed herewith.

Claims 1, 4-8 and 10-19 are pending. Claims 1, 4-8 and 10-19 previously were allowed. Claims 1, 4-8 and 11-19 are amended to correct formatting and typographical errors. No new matter is added.

* * *

In view of the amendment and remarks herein, allowance of the application respectfully is requested.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 0119378-00560 / 4207
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AMENDMENT PURSUANT TO 37 C.F.R. §1.312
DATED 07 OCTOBER 2009

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | | |
|---|---|---|---|
| Applicant | : Hamann *et al.* | Art Unit | : 1624 |
| Serial No. | : 10/712,456 | Examiner | : V. Balasubramanian |
| Filed | : November 13, 2003 | Confirm. No.: | 9300 |

Title : **OPEN-CHAIN PROLYL UREA-RELATED MODULATORS OF ANDROGEN RECEPTOR FUNCTION**

**Mail Stop ISSUE FEE**
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

**AMENDMENT PURSUANT TO 37 C.F.R. §1.312**

Dear Sir:

Entry of the following amendment and consideration of the following remarks respectfully are requested. This amendment is filed concurrently with the payment of the issue fee.

**Amendments to the Claims** begin on page 2 of this paper.

**Remarks** begin on page 10 of this paper.

A copy of the Supplemental Information Disclosure Statement, mailed April 9, 2009, is provided.

**CERTIFICATE OF MAILING BY "EXPRESS MAIL"**
"Express Mail" Mailing Label Number EM 315455134 US
Date of Deposit October 07, 2009
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Mail Stop Issue Fee, Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

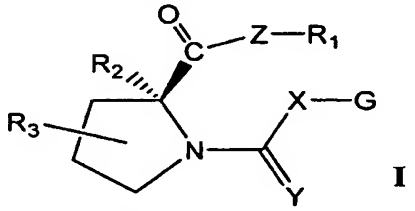
Stefanie S. Dost

**Amendments to the Claims:**

Please amend claims 1, 4, 5, 10 and 15 as follows. This listing of claims replaces all prior versions and listings of claims in the application.

**Listing of Claims:**

1. (Currently amended) A compound of ~~the~~ formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

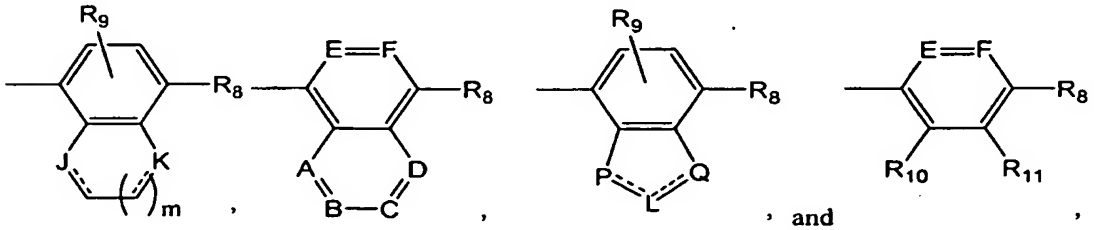
$R_1$ is selected from the group consisting of alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocycle or substituted heterocycle, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CH_2OR_4$, $OR_2$, $SR_2$, halo, $NHR_2$, $NHCOR_4$, and $NHCONR_4R_4'$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from ~~the group of~~ among:



, , , and ,

wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and $CR_1$;

J, K, L, P, and Q each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$;

m is an integer of 0 or 1 ;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and

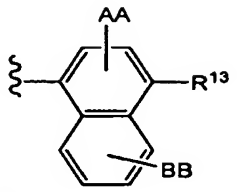
Z is –O– or $NR_4$;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_1$ is methyl,
X is NH, and
Y is O or S, then
Z is not O;

(c) when (i) $R_1$ is methyl,
(ii) X is NH,
(iii) Y is $NR_4$,
(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and
(v) G has the following structure:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-$NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, ~~$SO_2NR_{15}NR_{15}$'~~ $SO_2NR_{15}R_{15}$', $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group is independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

$R_{15}$ and $R_{15}$' in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and -CN;

AA and BB each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro (-$NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

2. and 3. (Cancelled).

4. (Currently amended) The compound of claim 1, or a pharmaceutically acceptable salt <u>of claim 1</u> ~~thereof,~~ wherein:

$R_1$ is alkyl;

$R_2$ is hydrogen or alkyl;

$R_3$ is hydroxyl;

<u>X is $NR_4$;</u>

Y is O; and

Z is O.

5. (Previously presented) A pharmaceutical composition, comprising:

a compound or salt of claim 1; and

a pharmaceutically acceptable carrier therefor.

6. (Previously presented) The pharmaceutical composition of claim 5, further comprising a growth promoting agent.

7. (Currently amended) A pharmaceutical composition, comprising:

a compound of claim 1, or a pharmaceutically acceptable salt ~~thereof,~~ of claim 1; and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

8. (Currently amended) A method for treating prostate cancer, comprising: administering to a mammalian species in need of treatment an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt ~~thereof~~of claim 1.

9 (Cancelled).

10. (Currently amended) A compound selected from the group consisting of

1-(4-Cyano-2-ethyl-3-(trifluoromethyl)phenyl-1-carbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid or a pharmaceutically acceptable salt thereof;

1-(4-Cyanonaphthalen-1-ylcarbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof;

1-(5-Chloro-6-cyano-pyridin-3-ylcarbamoyl)-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof; and

1-[2-(4-Cyanonaphthalen-1-yl)acetyl]-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof.

11. (Previously presented) A pharmaceutical composition, comprising:

a compound of claim 10, or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier therefor.

12. (Previously presented) The pharmaceutical composition of claim 11, further comprising a growth promoting agent.

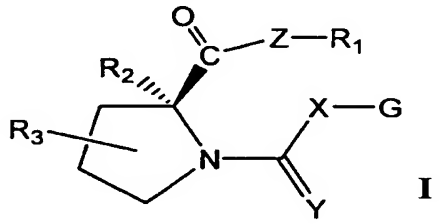
13. (Previously presented) A pharmaceutical composition, comprising:

a compound of claim 10, or a pharmaceutically acceptable salt thereof; and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

14. (Previously presented) A method for treating prostate cancer, comprising: administering to a mammalian species in need of treatment an effective amount of a compound of claim 10 or a pharmaceutically acceptable salt thereof.

15. (Currently amended) A compound of formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

$R_1$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

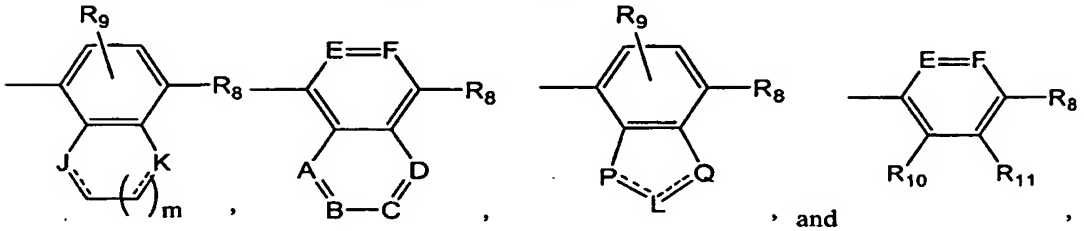
$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl and $CH_2OR_4$;

$R_3$ is selected from the group consisting of alkyl or substituted alkyl, and $CH_2OR_4$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or

substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from the group consisting of:




, , , and ,

wherein:

$R_8$ is CN;

$R_9$, $R_{10}$, and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and $CR_1$;

J, K, L, P, and Q each independently is selected from among $NR_{12}$, O, S, SO, $SO_2$ or $CR_{12}R_{12}'$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$;

m is an integer of 0 or 1 ;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$; and

Z is –O- or $NR_4$;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_1$ is methyl, X is NH, and Y is O or S, then Z is not O;

(c) when

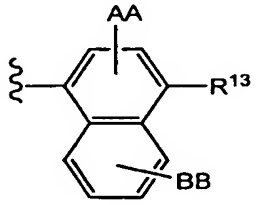
(i) $R_1$ is methyl,

(ii) X is NH,

(iii) Y is $NR_4$,

(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:




wherein:

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-$NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, ~~$SO_2NR_{15}NR_{15}$'~~ $\underline{SO_2NR_{15}R_{15}'}$, $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group ~~is~~ independently is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$ and $COR_{15}$;

$R_{15}$ and $R_{15}'$ in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and CN;

AA and BB each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro (-$NO_2$), alkyl or substituted alkyl and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

16. (Currently amended) A pharmaceutical composition, comprising:

a compound of claim 15, or a pharmaceutically acceptable salt ~~thereof~~ $\underline{\text{of claim 15}}$; and

a pharmaceutically acceptable carrier therefor.

17. (Previously presented) The pharmaceutical composition of claim 16, further comprising a growth promoting agent.

18. (Currently amended) A pharmaceutical composition, comprising:

a compound of claim 15, or a pharmaceutically acceptable salt ~~thereof~~ of claim 15; and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

19. (Currently amended) A method for treating prostate cancer, comprising:

administering to a mammalian species in need of treatment an effective amount of a compound of claim 15 or a pharmaceutically acceptable salt ~~thereof~~ of claim 15.

## REMARKS

The requisite fee of $1852.00 for payment of the Issue Fee for a large entity ($1510), publication fee ($300) and an advance order of 14 copies of the issued patent ($42), and any other fees that may be due in connection with this paper or this application during its entire pendency, should be charged to Deposit Account No. 02-1818. If a Petition for extension of time is needed, this paper is to be considered such Petition.

**Supplemental Information Disclosure Statement**

Pursuant to the Request of the Examiner, provided herein is a copy of a supplemental Information Disclosure Statement that was mailed April 9, 2009. Receipt of the Supplemental Disclosure Statement was acknowledged by the Office as evidenced by the date stamp on the first page, indicating the date of April 9, 2009. The Supplemental Information Disclosure Statement included a copy of an Office Action that issued in a related case, and a Table with a box for the Examiner to initial that the Examiner considered the Office Action. The Supplemental Information Statement was mis-coded in the system as a Transmittal Letter. Applicant's representative contacted Examiner Balasubramania, who requested that a copy of the Table be included with the Issue Fee. Examiner Balasubramania indicated that he would initial the table evidencing consideration of the Office Action from the related case.

**Amendment of the Claims**

Claims 1, 4-8 and 10-19 are allowed. Upon review of the claims in preparation of payment of the issue fee, it has been determined that claims 1, 4, 7, 8, 10, 16, 18 and 19 contain inadvertant errors, which are addressed by the amendments herein. Claim 1 is amended to correct grammatical errors by replacing the recitation "A compound of the formula I" with "A compound of formula I" and to amend the definition of substituent G by replacing the recitation "from the group of" with the recitation "from among." Claims 1 and 15 are amended to correct an inadvertant typographical error in the definition of substituent $R^{13}$, by replacing the recitation $SO_2NR_{15}NR_{15}$' with the recitation $SO_2NR_{15}R_{15}$'. Basis for this amendment is found in claim 1 as originally filed. Claim 4 is amended to include the recitation "X is $NR_4$." Basis for this amendment is found in original claim 4.

Claims 4, 7 and 8 are amended to replace the recitation "or a pharmaceutically acceptable salt *thereof*" with the recitation "or a pharmaceutically acceptable salt of claim 1" for proper dependency of the claims. Claims 4, 7 and 8 each ultimately depend from claim 1,

which recites "or a pharmaceutically acceptable salt *thereof*." Thus, claim 1 is directed to a compound of formula I or a pharmaceutically acceptable salt of a compound of formula I. Therefore, claims 4, 7 and 8 should recite "or a pharmaceutically acceptable salt of claim 1" for proper dependency.

Claim 10 is amended to correct a typographical error by inserting an omitted parenthesis in the second recited compound. Claim 10 is amended by replacing the recitation "1-(4-Cyanonaphthalen-1-ylcarbamoyl-3-hydroxy-pyrrolidine-2-carboxylic" with the recitation "1-(4-Cyanonaphthalen-1-ylcarbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic."

Claims 16, 18 and 19 are amended to replace the recitation "or a pharmaceutically acceptable salt *thereof*" with the recitation "or a pharmaceutically acceptable salt of claim 15" for proper dependency of the claims. Claims 16, 18 and 19 each ultimately depend from claim 15, which recites "or a pharmaceutically acceptable salt *thereof*." Thus, claim 15 is directed to a compound of formula I or a pharmaceutically acceptable salt of a compound of formula I. Therefore, claims 16, 18 and 19 should recite "or a pharmaceutically acceptable salt of claim 15" for proper dependency. No new matter is added. Accordingly, entry of this amendment respectfully is requested.

* * *

Entry of these remarks and the amendment into the file history of the above-captioned application respectfully is requested.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 3800024.00560 / 4207
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RESPONSE TO OFFICIAL ACTION AND AMENDMENT
DATED 18 APRIL 2008

CASE: 1073.134A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
Lawrence **HAMANN**, et al.
APPLICATION NO: 10/712,456
FILED: November 13, 2003
FOR: **OPEN CHAIN PROLYL UREA-RELATED MODULATORS OF ANDROGEN RECEPTOR FUNCTION**

ART UNIT: 1624
EXAMINER: **BALASUBRAMANIAN, VENKATARAMAN**

FILED VIA USPTO EFS-WEB
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO OFFICIAL ACTION

This is a response to the Official Action mailed January 24, 2008.

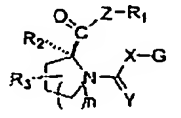
Amendments begin on page 2.

Remarks begin on page 10.

## CLAIM AMENDMENTS

Please amend the claims as follows. This listing of claims replaces all previous listings.

1 (Currently amended) A compound ~~or a pharmaceutically acceptable salt or a stereoisomer~~ of formula I



I

or a pharmaceutically acceptable salt thereof

wherein

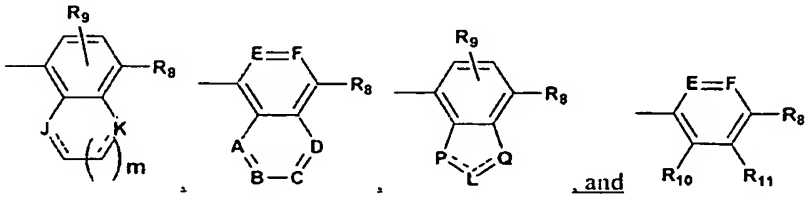
$R_1$ is selected from the group consisting of ~~hydrogen,~~ alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl, and $CH_2OR_4$;

$R_3$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CH_2OR_4$, $OR_2$, $SR_2$, halo, $NHR_2$, $NHCOR_4$, $NHCO_2R_4$, $NHCONR_4R_4'$, and $NHSO_2R_4$;

$R_4$ and $R_4'$ for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, and heteroaryl or substituted heteroaryl;

G is selected from the group consisting of:



, and

wherein

$R_8$ is CN;

$R_9$, $R_{10}$ and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4'$, $CONR_4R_4'$, $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteraryl;

A to F ~~is~~ are each independently selected from N ~~or~~ and $CR_1$;

J, K, L, P and Q are each independently selected from $NR_{12}$, O, S, SO, $SO_2$, or $CR_{12}R_{12'}$;

$R_{12}$ and $R_{12}'$ in each functional group are each independently selected from a bond or $R_1$; ~~and~~

m is an integer of 0 or 1;

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$;

Z is -O- or $NR_4$; and

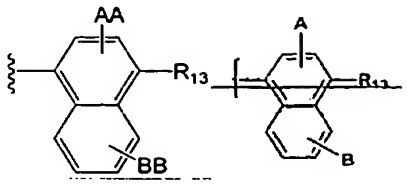
n is an integer of 1 or 2;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) ~~excluding compounds where the following occur simultaneously:~~ when $R_1$ is methyl~~;~~, X is NH~~;~~, and Y is O or S~~;~~, ~~and~~ then Z is not O;

(c) when ~~excluding compounds where the following occur simultaneously:~~ (i) $R_1$ is methyl~~;~~, (ii) X is NH~~;~~, ~~Z is O;~~ (iii) Y is $NR_4$~~;~~, (iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl~~;~~, and (v) G has the following structure:




wherein

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-$NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, $SO_2NR_{15}R_{15}'$, $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group is independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$, and $COR_{15}$;

$R_{15}$ and $R_{15}'$ in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl, and -CN;

AA and BB are each independently selected from the group consisting of hydrogen, halo, cyano(-CN), nitro(-$NO_2$), alkyl or substituted alkyl, and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

2. (cancelled)

3 (cancelled)

4. (Currently amended) The compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, wherein

$R_1$ is ~~hydrogen or~~ alkyl;

$R_2$ is hydrogen or alkyl;

$R_3$ is hydroxyl;

X is $NR_4$;

Y is O;

Z is O;

and n is 1

5. (Currently amended) A pharmaceutical composition comprising ~~the~~ a compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefore.

6. (Original) The pharmaceutical composition as defined in claim 5 further comprising a growth promoting agent.

7. (Currently amended) A pharmaceutical composition comprising a compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, and at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, anti-osteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

8. (Currently amended) A method for treating prostate cancer which comprises administering to a mammalian species in need of treatment an effective amount of a compound as defined in claim 1 or a pharmaceutically acceptable salt thereof.

9.(cancelled)

10. (Currently amended) A compound selected from the group consisting of 1-(4-Cyano-2-ethyl-3-(trifluoromethyl)phenyl-1-carbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof;

1-(4-Cyanonaphthalen-1-ylcarbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof;

1-(5-Chloro-6-cyano-pyridin-3-ylcarbamoyl)-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof; and

1-[2-(4-Cyanonaphthalen-1-yl)acetyl]-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof.

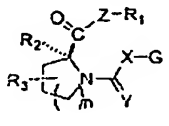
11. (new) A pharmaceutical composition comprising the a compound as defined in claim 10, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

12. (new) The pharmaceutical composition as defined in claim 11 further comprising a growth promoting agent.

13 (new) A pharmaceutical composition comprising a compound as defined in claim 10, or a pharmaceutically acceptable salt thereof, and at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, anti-osteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

14. (new)A method for treating prostate cancer which comprises administering to a mammalian species in need of treatment an effective amount of a compound as defined in claim 10 or a pharmaceutically acceptable salt thereof.

15. (new) A compound of formula I



I

or a pharmaceutically acceptable salt thereof

wherein

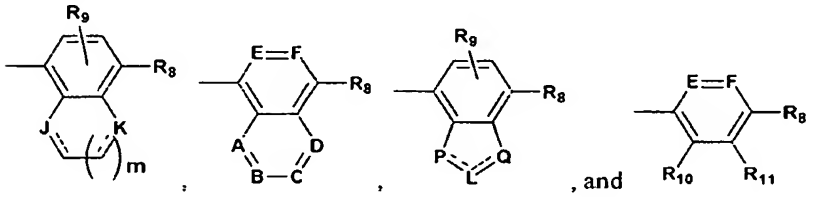
$R_1$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and $CH_2OR_4$;

$R_2$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl, and $CH_2OR_4$;

$R_3$ is selected from the group consisting of alkyl or substituted alkyl, and $CH_2OR_4$;

$R_4$ and $R_4$' for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, and heteroaryl or substituted heteroaryl;

G is selected from the group consisting of:



wherein

$R_8$ is CN;

$R_9$, $R_{10}$ and $R_{11}$ are each independently selected from the group consisting of hydrogen (H), $NO_2$, CN, $CF_3$, $OR_4$, $CO_2R_4$, $NR_4R_4$', $CONR_4R_4$', $CH_2OR_4$, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteraryl;

A to F are each independently selected from N and $CR_1$;

J, K, L, P and Q are each independently selected from $NR_{12}$, O, S, SO, $SO_2$, or $CR_{12}R_{12'}$;

$R_{12}$ and $R_{12}$' in each functional group are each independently selected from a bond or $R_1$,

m is an integer of 0 or 1,

X is a linking group selected from the group consisting of $NR_4$ and $CHR_4$;

Y is selected from the group consisting of O, $NR_4$, $NOR_4$, S and $CH_2$;

Z is -O- or $NR_4$; and

n is an integer of 1 or 2;

with the following provisos:

(a) when Y is $NOR_4$, $R_4$ is not hydrogen;

(b) when $R_1$ is methyl, X is NH, and Y is O or S, then Z is not O;

(c) when

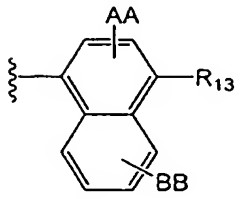
(i) $R_1$ is methyl,

(ii) X is NH,

(iii) Y is $NR_4$,

(iv) $R_4$ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:




wherein

$R_{13}$ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-$NO_2$), halo, heterocyclo, $OR_{14}$, $CO_2R_{15}$, $CONHR_{15}$, $COR_{15}$, $S(O)_pR_{15}$, $SO_2NR_{15}R_{15}'$, $NHCOR_{15}$ and $NHSO_2R_{15}$;

$R_{14}$ in each functional group is independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, $CHF_2$, $CF_3$, and $COR_{15}$;

$R_{15}$ and $R_{15}'$ in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl,

arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl, and -CN;

AA and BB are each independently selected from the group consisting of hydrogen, halo, cyano(-CN), nitro(-$NO_2$), alkyl or substituted alkyl, and $OR_{14}$; and

p is an integer from 0 to 2,

then Z is not O.

16. (new) A pharmaceutical composition comprising the a compound as defined in claim 15, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

17. (new) The pharmaceutical composition as defined in claim 16 further comprising a growth promoting agent.

18. (new) A pharmaceutical composition comprising a compound as defined in claim 15, or a pharmaceutically acceptable salt thereof, and at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, anti-osteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

19. (new) A method for treating prostate cancer which comprises administering to a mammalian species in need of treatment an effective amount of a compound as defined in claim 15 or a pharmaceutically acceptable salt thereof.

REMARKS

Claims 1, 4-8, and 10-19 are pending in the application. Claims 1, 4, 5, 7, 8 and 10 are amended in this response; claims 11-19 are new. In the Official Action mailed January 24, 2008, the Examiner rejected claims 1, 4 and 5 as being anticipated by Sun et al., US 2004/0019063 per 35 U.S.C. §102(e), and rejected claims 1, 4, 5 and 10 as being obvious in view of Sun et al. The Examiner also stated that claims 6-8 were not allowable because they depended from a rejected base claim but would be allowable if rewritten in independent form.

Before explaining the present amendments and responding to the anticipation rejection, Applicants note that at the time the presently claimed invention was invented, the Applicants were under a duty to assign to the same assignee of record in the '063 publication, viz. Bristol-Myers Squibb Company. Consequently, under 35 U.S.C. §103(c), **the '063 publication cannot be cited against the present application as the basis for a §103 obviousness rejection.**

Claim 1

Claim 1 has been amended to delete the recitation that formula I includes stereoisomers, inasmuch as, to the extent that the stereochemistry of the molecule is not depicted in formula I, formula I by definition encompasses all stereoisomers. See e.g. paragraph 101 of the published specification. Additional amendments have also been made in claim 1 for the sake of clarity, e.g. the definition of G has been amended to more clearly recite that G is selected from the group consisting of the four structures shown, and the definition of substituents A-F has been amended to more clearly recite that each of A-F is independently selected from N and $CR_1$. Provisos (b) and (c) have been amended to more clearly recite what is excluded from the claim. Also, in the structure for G shown in proviso (c), the substituents on the naphthalene moiety have been renamed AA and BB, so as to avoid confusion with the substituents A and B recited earlier in the claim. Finally, in claim 1, the definition of $R_1$ has been amended to exclude H. It is respectfully submitted that none of these amendments introduce new matter.

In the Official Action, the Examiner asserted that formula Ih in the '063 publication shows a genus of compounds that include some of the presently claimed compounds. Applicants respectfully submit that the Examiner is mistaken in this conclusion, since proviso (b) of claim 1, both as originally filed and in its present form, excludes from claim 1 the prolyl methyl esters of formula Ih of the '063 publication, as well as compounds of formula IVa of the '063 publication.

Furthermore, it is respectfully submitted that in view of the deletion of H from the definition of $R_1$ in claim 1 (as now amended), compounds such as compounds of formula XIX or the compound shown in Example 54B of the '063 publication are no longer within the scope of present claim 1. It is thus submitted that there are no compounds disclosed in the '063 publication that fall within the scope of claim 1, and therefore claim 1 is novel over the '063 publication.

Since, as noted above, the '063 publication is not available as prior art for purposes of an obviousness rejection against the present application, Applicants believe there is no longer a basis for rejection of claim 1, and allowance of this claim is respectfully requested.

Claim 4

Claim 4 depends from claim 1. In accordance with the amendments in claim 1, the definition of $R_1$ in claim 4 has been amended so that H is no longer recited. This claim has also been amended to clarify that pharmaceutically acceptable salts are within the scope of the claim.

Claim 5

Claim 5 has been amended to clarify that the pharmaceutical composition includes a compound according to claim 1 or a pharmaceutically acceptable salt thereof, not "the" compound of claim 1. A typographical error in the word "therefor" has also been corrected.

Claims 7, 8 and 10

Claims 7, 8 and 10 have been amended to clarify that they include pharmaceutically acceptable salts of the recited compounds.

New claims 11-14

New claims 11-14 correspond to claims 5-8, but refer to the compounds or salts recited in claim 10 rather than the compounds or salts recited in claim 1.

New claims 15-19

New claim 15 corresponds to claim 1 as filed in on August 29, 2007, but the definition of $R_3$ has been limited to alkyl, substituted alkyl and $CH_2OR_4$. It is respectfully submitted that this

limitation, in combination with proviso (b), excludes from claim 15 compounds of formulae Ih, IVa, XIX or Example 54B of the '063 publication, and therefore this claim is novel over that publication. Since, as explained above, the '063 publication cannot be used against the present application as a §103 reference, it is respectfully submitted that new claim 15 is allowable. New claims 16-19 correspond to claims 6-9 but refer to the compounds or salts recited in claim 15 rather than the compounds or salts recited in claim 1.

In view of the foregoing amendments and remarks, it is submitted that the application is in condition for allowance. Allowance thereof is respectfully requested.

Sincerely yours,

Daniel J. Feigelson
Applicants' representative

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| **EFS ID:** | 3173053 |
| **Application Number:** | 10712456 |
| **International Application Number:** | |
| **Confirmation Number:** | 9300 |
| **Title of Invention:** | Open chain prolyl urea-related modulators of androgen receptor function |
| **First Named Inventor/Applicant Name:** | Lawrence G. Hamann |
| **Customer Number:** | 23405 |
| **Filer:** | Daniel J. Feigelson |
| **Filer Authorized By:** | |
| **Attorney Docket Number:** | 1073.134A |
| **Receipt Date:** | 18-APR-2008 |
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